

### **REMARKS**

This responds to the Office Action mailed on May 17, 2005. Claims 1, 6, 11 and 16-27 been cancelled without prejudice to their prosecution in a continuation or divisional application. As a result claims 2-5, 7-10 and 12-15 are pending in this application.

#### ***Personal Interview***

Applicant wishes to thank the Examiner for extending the courtesy of a telephone interview to Applicant's representative, Robin A. Chadwick, on August 10, 2005.

The issues raised in the Office Action were discussed. The Examiner suggested that claim 2 might be patentable if a further examination of the prior art did not indicate otherwise.

This account is believed to be a complete and accurate summary of the interview as required by 37 C.F.R. § 1.133. If the Examiner believes that this summary is inaccurate or incomplete, Applicants respectfully request that the Examiner point out any deficiencies in his next communication so that Applicants can amend or supplement the interview summary.

#### ***§112 Rejection of the Claims***

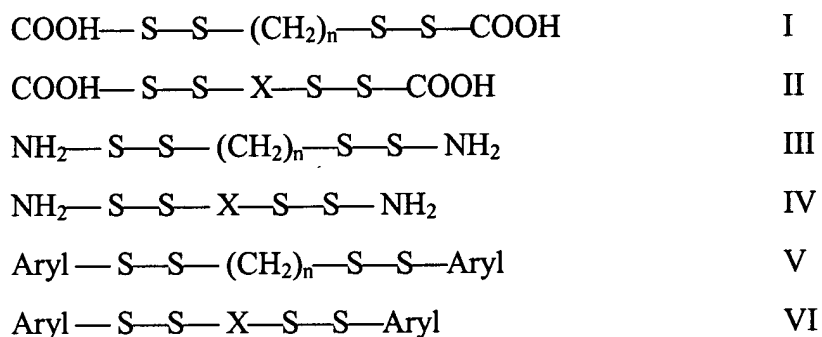
Claims 1, 6 and 11 were rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement for a generic crosslinker that can form a pore upon exposure to a reducing agent. The Examiner stated that the specification does enable disulfide crosslinkers. Claims 1, 6 and 11 have been cancelled without prejudice to their prosecution in a continuation or divisional application. Applicant respectfully requests withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

#### ***§103 Rejection of the Claims over Steiner, Mathiowitz and Margolin***

Claims 1-15 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Steiner (U.S. Patent No. 4,925,673) in combination with Mathiowitz (U.S. Patent No. 5,271,961) and Margolin (U.S. Patent No. 6,541,606). According to the Examiner, Steiner discloses proteinoid delivery systems of thermally condensed amino acids but lacks a teaching on crosslinking using disulfide bridges, however, the Examiner asserts that Mathiowitz discloses

protein microspheres with cross-linking agents such as glutaraldehyde and Margolin discloses thio-labile linkers having the structure R'-S-S-R.

Claims 1, 6 and 11 have been cancelled without prejudice to their prosecution in a continuation or divisional application. Claim 2 is directed to a proteinoid microsphere comprising a mixture of amino acids that are thermally condensed and crosslinked with a crosslinker of any one of formulae I-VI.



wherein:

X is a spacer group of about approximately 3 to 100 angstroms by about 2 to 30 angstroms that comprises an alkane chain, an alkene chain, a cycloalkyl or aryl ring having five to fourteen carbon atoms, or a combination thereof;

n is an integer ranging from 1 to 18;

S is a sulfur atom; and

Aryl is a phenyl radical or an ortho-fused bicyclic radical having about nine to ten ring atoms wherein at least one ring is aromatic and wherein each Aryl moiety is substituted with at least one reactive group that can form a covalent linkage with an amino acid.

Claims 7 and 12 are similarly directed to compositions and articles for wound treatment that include such proteinoid microspheres.

Applicant submits that none of the cited references teach the crosslinkers of claims 2-5, 7-10 and 12-15. Steiner provides no teaching on crosslinkers whatsoever. Mathiowitz is limited to disclosure of crosslinkers such as glutaraldehyde and provides no disclosure or suggestion of

disulfide crosslinkers. Margolin is limited to generic disclosure of R'-S-S-R reagents for use with protein crystals and therefore does not disclose the invention, which relates to proteinoid microspheres crosslinked with a crosslinker of any one of formulae I-VI.

Moreover, one of skill in the art would actually be discouraged from using disulfide cross-linking agents with thermally condensed proteinoid microspheres after consulting the combination of documents cited by the Examiner. Steiner is the only reference that discloses thermally condensed microspheres but it provides no teaching or suggestion that crosslinking agents should be employed with those proteinoid microspheres. Neither of Mathiowitz nor Margolin discloses nor teaches use of thermally condensed proteinoid microspheres with cross-linking agents. While Mathiowitz and Margolin do disclose some crosslinking agents, the crosslinking procedures described in involve gentle exposure of proteins to the crosslinking agent at room temperature (see Margolin, col. 51-52; Mathiowitz, col. 6, lines 54-62). Neither Margolin nor Mathiowitz suggest use of crosslinkers while using the high temperatures needed for thermally condensing amino acids into proteinoid microspheres. Instead, Margolin and Mathiowitz advocate use of mild conditions and temperatures. For example, Mathiowitz specifically states that proteins should be modified (e.g. cross-linked) before microsphere formation because "an advantages of the phase separation process [employed to make the protein microspheres] is that harsh chemical or heat treatment after formation of the microspheres is not required." Thus, one of skill in the art would conclude from the combination of references that crosslinkers should not be used during thermal condensation of amino acids into proteinoid microspheres.

Applicant submits that the claims are non-obvious and patentable over the combination of Steiner, Mathiowitz and Margolin, and respectfully requests withdrawal of this rejection of claims 1-15 under 35 USC § 103(a).

***§103 Rejection of the Claims over Steiner, Mathiowitz Margolin and McKenzie***

Claims 1-15 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Steiner (U.S. Patent No. 4,925,673) in combination with Mathiowitz (U.S. Patent No. 5,271,961), Margolin (U.S. Patent No. 6,541,606) and McKenzie (J. Biol. Chem. 275: 9970-77

(2000)). In addition to the teachings of Steiner, Mathiowitz and Margolin, the Examiner further alleges that McKenzie teaches that the cell has a reducing environment.

Applicant submits that McKenzie does not cure the defects of Steiner, Mathiowitz and Margolin, which include no disclosure of a proteinoid microspheres made from thermally condensed amino acids in the presence of the claimed disulfide crosslinkers (see further discussion of these defects above). Instead, McKenzie is limited to insertion of multiple cysteine residues into short synthetic peptides and combination of those peptides with DNA to form a peptide gene delivery agent. Nowhere does McKenzie disclose proteinoid microspheres made from thermally condensed amino acids in the presence of a disulfide crosslinker. Absent a teaching of all the elements of the present claims Applicant submits that the combination of references cited cannot anticipate or render obvious the claims.

Moreover, Applicant submits that one of skill in the art would not be motivated to modify the cited references to find the present invention. As explained above, only Mathiowitz and Margolin provide any disclosure of a crosslinking agent and the agents disclosed are not the crosslinkers of the present invention. McKenzie discloses peptides with cysteine residues. Even if the cysteine-containing peptides of McKenzie were somehow construed to be crosslinking agents, those cysteine-containing peptides are not the crosslinkers of the present invention. Moreover, if the cysteine-containing peptides of McKenzie were somehow construed to be crosslinking agents, each of Mathiowitz, Margolin and McKenzie all advocate mild conditions when combining their "cross-linking agents" with proteins or DNA. None of the references cited disclose or teach thermally condensing amino acids with a crosslinker to form a proteinoid microsphere.

Applicant submits that the claims are non-obvious and patentable over the combination of Steiner, Mathiowitz, Margolin and McKenzie, and respectfully requests withdrawal of this rejection of claims 1-15 under 35 USC § 103(a).

**CONCLUSION**

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (516) 795-6820 to facilitate prosecution of this application.

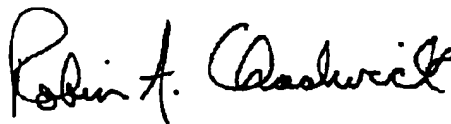
If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

STEPHEN QUIRK

By his Representatives,

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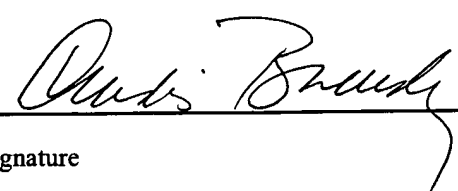
Date August 16, 2005

By \_\_\_\_\_  
Robin A. Chadwick  
Reg. No. 36,477

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Mail Stop Amendment, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 16th day of August, 2005.

**CANDIS BUENDING**

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Name

  
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